1 (Currently Amended): A prepared heterogeneous DNA segment for placement in an expression vector capable of effecting transfection of endothelial cells in-situ such that overexpression of extracellular matrix heparan sulphate proteoglycans subsequently occurs in-situ, said prepared heterogeneous DNA segment comprising:

at least one first DNA sequence coding for the extracellular domain of a recombinant proteoglycan entity that is not a naturally occurring form of a syndecan-4 molecule, and which can be expressed by a transfected endothelial cell in-situ after being transfected with an expression vector carrying said first DNA sequence, said extracellular domain first DNA sequence specifying the extracellular N-terminal portion of said expressed recombinant proteoglycan entity which then extends from the endothelial cell surface and is capable of binding heparan sulfates to form an extracellular matrix in-situ;

at least one second DNA sequence coding for the transmembrane domain of said recombinant proteoglycan entity that is not a naturally occurring form of a syndecan-4 molecule, and which can be expressed by a transfected endothelial cell in-situ after being transfected with an expression vector carrying said second DNA sequence, said transmembrane domain second DNA sequence specifying the medial portion of said expressed recombinant proteoglycan entity which then extends through the endothelial cell membrane and is joined with said

extracellular N-terminal portion of said expressed recombinant proteoglycan entity; and

at least one third DNA sequence coding for the cytoplasmic domain of a syndecan-4 molecule in said recombinant proteoglycan entity, and which can be expressed by a transfected endothelial cell in-situ after being transfected with an expression vector carrying said third DNA sequence, said syndecan-4 cytoplasmic domain third DNA sequence specifying the cytoplasmic portion of said expressed recombinant proteoglycan entity which is then present within the cytoplasm of a transfected endothelial cell and is joined to said transmembrane portion of said expressed recombinant proteoglycan entity.

2 (Currently Amended): A constructed expression vector capable of effecting transfection of endothelial cells in-situ such that overexpression of extracellular matrix heparan sulfate proteoglycan subsequently occurs in-situ, said constructed expression vector comprising:

a prepared heterogeneous DNA segment comprised of

(I) at least one first DNA sequence coding for the extracellular domain a recombinant proteoglycan entity that is not a naturally occurring form of a syndecan-4 molecule, and which can be expressed by a transfected endothelial cell in-situ after being transfected with an expression vector carrying said first DNA sequence, said extracellular

domain first DNA sequence specifying the extracellular N-terminal portion of said expressed recombinant proteoglycan entity which then extends from the endothelial cell surface and is capable of binding heparan sulfates to form an extracellular matrix in-situ,

(ii) at least one second DNA sequence coding for the transmembrane domain of said recombinant proteoglycan entity that is not a naturally occurring form of a syndecan-4 molecule, and which can be expressed by a transfected endothelial cell in-situ after being transfected with an expression vector carrying said second DNA sequence, said transmembrane domain second DNA sequence specifying the medial portion of said expressed recombinant proteoglycan entity which then extends through the endothelial cell membrane and is joined with said extracellular N-terminal portion of said recombinant proteoglycan entity, and

(iii) at least one third DNA sequence coding for the cytoplasmic domain of a syndecan-4 molecule in said recombinant proteoglycan entity, and which can be expressed by a transfected endothelial cell in-situ after being transfected with an expression vector carrying said third DNA sequence, said syndecan-4 cytoplasmic domain third DNA sequence specifying the cytoplasmic portion of said expressed recombinant proteoglycan entity which is then present within the cytoplasm of a transfected endothelial cell and is joined to said

transmembrane portion of said expressed recombinant proteoglycan entity; and

an expression vector carrying said prepared heterogeneous DNA segment and capable of effecting transfection of endothelial cells in-situ.

3 (Currently Amended): An in-situ transfected endothelial cell which ~~comprises~~ exists as a part of a living tissue in vitro, overexpresses extracellular matrix heparan sulfate recombinant proteoglycans, and positions the recombinant proteoglycans at the endothelial cell surface, said in-situ transfected endothelial cell comprising:

a viable endothelial cell transfected in-situ with a constructed expression vector such that said transfected endothelial cell overexpresses extracellular matrix heparan sulfate recombinant proteoglycan entities that are not a naturally occurring form of a syndecan-4 molecule, said overexpressed recombinant proteoglycan entities being comprised of

(I) an extracellular N-terminal portion for said recombinant proteoglycan entity that is not a naturally occurring form of a syndecan-4 molecule and which extends from the transfected endothelial cell surface and binds heparan sulfates to form an extracellular matrix in-situ, said extracellular N-terminal portion being the expressed product of at least one first DNA sequence carried by the constructed expression vector and

coding for the extracellular domain of said recombinant proteoglycan entity expressed by the transfected endothelial cell in-situ,

(ii) a transmembrane medial portion for said recombinant proteoglycan entity that is not a naturally occurring form of a syndecan-4 molecule and which extends through the endothelial cell membrane and is joined with said extracellular N-terminal portion of said recombinant proteoglycan entity, said transmembrane medial portion being the expressed product of at least one second DNA sequence carried by the constructed expression vector and coding for the transmembrane domain of said recombinant proteoglycan entity expressed by the transfected endothelial cell in-situ, and

(iii) a syndecan-4 cytoplasmic portion for said recombinant proteoglycan entity which is present within the cytoplasm of the transfected endothelial cell and is joined to said transmembrane portion of said recombinant proteoglycan entity, said syndecan-4 cytoplasmic portion being the expressed product of at least one third DNA sequence carried by the constructed expression vector and coding for the cytoplasmic domain of the syndecan-4 molecule of said recombinant proteoglycan entity expressed by the transfected endothelial cell in-situ.

4 (Previously Amended): The prepared heterogeneous DNA segment as recited by claim 1 wherein said first DNA sequence coding for the

extracellular domain of said recombinant proteoglycan entity is selected from the group consisting of syndecan DNA sequences, glypican DNA sequences and perlecan DNA sequences.

5 (Previously Amended): The prepared heterogeneous DNA segment as recited by claim 1 wherein said second DNA sequence coding for the transmembrane domain of said recombinant proteoglycan entity is selected from the group consisting of syndecan DNA sequences, glypican DNA sequences and perlecan DNA sequences.

6 (Previously Amended): The constructed expression vector as recited by claim 2 wherein said expression vector capable of effecting transfection of endothelial cells in-situ is a plasmid.

7 (Previously Amended): The constructed expression vector as recited by claim 2 wherein said expression vector capable of effecting transfection of endothelial cells in-situ is a virus.

8 (Original). The in-situ transfected endothelial cell as recited by claim 3 wherein said cell is selected from the group consisting of vascular endothelial cells and dermal endothelial cells.

9 (Cancelled). [The in-situ transfected endothelial cell as recited by claim 3 wherein said cell exists under in-vivo conditions.]

10 (Cancelled). [The in-situ transfected endothelial cell as recited by claim 3 wherein said cell exists under in-vitro conditions.]

11 (Original). The in-situ transfected endothelial cell as recited by claim 3 wherein said transfected endothelial cell exists in a tissue comprising at least one kind of muscle cell selected from the group consisting of myocardial muscle cells, smooth muscle cells and striated muscle cells.

12 (Currently Amended): A method for making a prepared heterogeneous DNA segment intended for placement in an expression vector capable of effecting transfection of endothelial cells in-situ such that overexpression of extracellular matrix heparan sulfate recombinant proteoglycan entities occurs in-situ, said method comprising the steps of:

obtaining at least one first DNA sequence coding for the extracellular domain of a recombinant proteoglycan entity that is not a naturally occurring form of a syndecan-4 molecule, and which can be expressed by a transfected endothelial cell in-situ after being transfected with an expression vector carrying said first DNA sequence, said extracellular

domain first DNA sequence specifying the extracellular N-terminal portion of said expressed recombinant proteoglycan entity which then extends from the transfected endothelial cell surface and is capable of binding heparan sulfates to form an extracellular matrix in-situ;

acquiring at least one second DNA sequence coding for the transmembrane domain of said recombinant proteoglycan entity that is not a naturally occurring form of a syndecan-4 molecule, and which can be expressed by a transfected endothelial cell in-situ after being transfected with an expression vector carrying said second DNA sequence, said transmembrane domain second DNA sequence specifying the medial portion of said expressed recombinant proteoglycan entity which then extends through the transfected endothelial cell membrane and is joined with said extracellular N-terminal portion of said expressed recombinant proteoglycan entity;

procuring at least one third DNA sequence coding for the cytoplasmic domain of a syndecan-4 molecule in said recombinant proteoglycan entity, and which can be expressed by a transfected endothelial cell in-situ after being transfected with an expression vector carrying said third DNA sequence, said syndecan-4 cytoplasmic domain third DNA sequence specifying the cytoplasmic portion of said expressed recombinant proteoglycan entity which is then present within the cytoplasm of an transfected endothelial cell and is joined to said

transmembrane portion of said expressed recombinant proteoglycan entity; and

joining together said extracellular domain first DNA sequence, said transmembrane domain second DNA sequence, and said syndecan-4 cytoplasmic domain third DNA sequence as a prepared heterogeneous DNA segment.

13 (Currently Amended): A method for making a constructed expression vector capable of effecting transfection of endothelial cells in-situ such that overexpression of extracellular matrix heparan sulfate recombinant proteoglycan entities subsequently occurs in-situ, said method comprising the steps of:

obtaining a prepared heterogeneous DNA segment comprised of

(I) at least one first DNA sequence coding for the extracellular domain of a recombinant proteoglycan entity that is not a naturally occurring form of a syndecan-4 molecule, and which can be expressed by a transfected endothelial cell in-situ after being transfected with an expression vector carrying said first DNA sequence, said extracellular domain first DNA sequence specifying the extracellular N-terminal portion of said expressed recombinant proteoglycan entity which then extends from the transfected endothelial cell surface and is capable of binding heparan sulfates to form an extracellular matrix in-situ,

(ii) at least one second DNA sequence coding for the transmembrane domain of said recombinant proteoglycan entity that is not a naturally occurring form of a syndecan-4 molecule, and which can be expressed by a transfected endothelial cell in-situ after being transfected with an expression vector carrying said second DNA sequence, said transmembrane domain second DNA sequence specifying the medial portion of an expressed proteoglycan entity which then extends through the transfected endothelial cell membrane and is joined with said extracellular N-terminal portion of said expressed recombinant proteoglycan entity, and

(iii) at least one third DNA sequence coding for the cytoplasmic domain of the syndecan-4 molecule in said recombinant proteoglycan entity, and which can be expressed by a transfected endothelial cell in-situ after being transfected with an expression vector carrying said third DNA sequence, said syndecan-4 cytoplasmic domain third DNA sequence specifying the cytoplasmic portion of an expressed proteoglycan entity which is then present within the cytoplasm of said transfected endothelial cell and is joined to said transmembrane portion of said expressed recombinant proteoglycan entity; and

positioning said prepared heterogeneous DNA segment into an expression vector suitable for transfection of endothelial cells in-situ.

14 (Cancelled). [A method for stimulating angiogenesis in-situ within living tissues comprising vascular endothelial cells, said method comprising the steps of:

transfecting vascular endothelial cells in-situ with a constructed expression vector such that the resulting transfected vascular endothelial cells overexpress discrete extracellular matrix heparan sulphate proteoglycan entities coded for by said constructed expression vector, said overexpressed proteoglycan entities being comprised of

(I) an extracellular N-terminal portion which is located at and extends from a transfected vascular endothelial cell surface and binds heparan sulphates to form an extracellular matrix in-situ, said extracellular N-terminal portion being the expressed product of at least one first DNA sequence in the constructed expression vector coding for the extracellular domain in a proteoglycan entity expressed by a transfected vascular endothelial cell in-situ after being transfected with said first DNA sequence,

(ii) a transmembrane medial portion which is located at and extends through a transfected vascular endothelial cell membrane and is joined with said extracellular N-terminal portion of said expressed proteoglycan entity, said transmembrane medial portion being the expressed product of at least one second DNA sequence in the constructed expression vector coding for the transmembrane domain of

said proteoglycan entity expressed by a transfected vascular endothelial cell in-situ after being transfected with said second DNA sequence, and

(iii) a syndecan-4 cytoplasmic portion present within the cytoplasm of a transfected vascular endothelial cell which is joined to said transmembrane portion and said extracellular N-terminal portion of said expressed proteoglycan entity, said syndecan-4 cytoplasmic portion being the expressed product of at least one third DNA sequence in the constructed expression vector coding for the cytoplasmic domain of the syndecan-4 molecule of said proteoglycan entity expressed by a transfected vascular endothelial cell in-situ after being transfected with said third DNA sequence; and

allowing said transfected vascular endothelial cells bearing said overexpressed extracellular matrix proteoglycan entities to stimulate angiogenesis in-situ.]

15 (Cancelled). [The method for stimulating angiogenesis in-situ as recited by claim 14 wherein said living tissue comprises at least one other type of cell selected from the group consisting of muscle cells, fibrocytes and fibroblasts, epithelial cells, osteocysts and osteoblasts, erythrocytes and leukocytes, and neurons.]

16 (Cancelled). [The method for stimulating angiogenesis in-situ as recited by claim 14 wherein said living tissue comprises at least one tissue selected from the group consisting of myocardium, lung, brain, kidney, spleen, liver, and gastro-intestinal tissues.]

17 (Cancelled). [The method for stimulating angiogenesis in-situ as recited by claim 14 wherein said living tissue comprising vascular endothelial cells is transfected using means selected from the group consisting of catheter-based administration, injection-based administration, infusion-based administration, localized intravascular deliveries, liposome-based deliveries, and administrations using target-directed peptides.]

18 (Cancelled). [The method for stimulating angiogenesis in-situ as recited by claim 14 wherein said method is practiced under in-vivo conditions.]

19 (Cancelled). [The method for stimulating angiogenesis in-situ as recited by claim 14 wherein said method is practiced under in-vitro conditions.]

Applicants have addressed each item of non-compliance as stated in the Notice forthrightly and objectively. In applicants' view, each defect controversy has been resolved completely. For these reasons, applicants respectfully submit and affirm that the presently pending claims 1-8 and 11-13 as well as non-pending claims 9-10 and 14-19 now comply with the requirements of 37 C.F.R. 121.

Respectfully submitted,

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